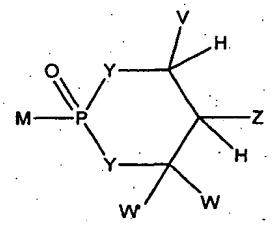
## *Amendments to the Claims*

The listing of claims will replace all prior versions, and listings of claims in the application.

1. (Currently Amended) A compound of formula I:




I

wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V; or

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy,

alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus; or

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl; or

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl; or

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH^2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2$NHaryl, $(CH_2)_p$-$OR^{12}$, and $-(CH_2)_p$-$SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

$R^2$ is selected from the group consisting of $R^3$ and -H;

$R^3$ is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

$R^6$ is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

$R^{12}$ is selected from the group consisting of -H, and lower acyl;

one Y is -O- and the other Y is $-NR^6$-;

M is selected from the group that attached to $PO_3^{2}$, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent ~~but is not an FBPase inhibitor,~~ and is attached to the phosphorus in ~~formula~~ Formula I via a carbon, oxygen, sulfur or nitrogen atom;

~~with the provisos that:~~

~~1) M is not NH(lower alkyl), N(lower alkyl)$_2$, NH(lower alkylhalide), N(lower alkylhalide)$_2$, or N(lower alkyl) (lower alkylhalide); and~~

~~2) $R^6$ is not lower alkylhalide;~~

and pharmaceutically acceptable prodrugs and salts thereof, wherein:

said prodrug is an alkyl, aryl, aralkyl, acyloxyalkyl or alkoxycarbonyloxyalkyl ester of a -COOH group on Formula I, or an acyl group, alkoxycarbonyl, aminocarbonyl, phosphate or sulfate group condensed with a -OH, -SH, -NH- or -$NH_2$ group on Formula I.

2.-3. (Cancelled).

4. (Currently Amended) The compounds of ~~claim 174~~ claim 1 wherein ~~MH is~~ M is the residue of a compound selected from the group consisting of L-deoxycytidine (LdC), L-thymidine (LdT), 9-beta-D-arabinofuranosyladenine (araA), azidothymidine (AZT), stavudine (d4T), didanosine (ddI), 2',3'-dideoxyadenosine (ddA), 2',3'-dideoxycytidine (ddC), L-2',3'-dideoxycytidine (L-ddC), L-2',3'-dideoxyfluorocytidine (L-FddC), L-2',3'-dideoxy-2',3'-didehydrocytidine (L-d4C), L-2',3'-dideoxy-2',3'-didehydro-5-fluorocytidine (L-Fd4C), lamuvidine (3TC), ~~LdC, LdT, araA, AZT, d4T, ddI, ddA, ddC, L-ddC, L-FddC, L-d4C, L-Fd4C, 3TC,~~ ribavirin, penciclovir, 5-fluoro-2'-

deoxyuridine, fialuridine (FIAU), fiacitabine (FIAC), (±)-(1α,2β,3α)-9-[2,3-bis(hydroxymethyl)cyclobutyl]-guanine (BHCG), ~~FIAU, FIAC, BHCG,~~ 2'R,5'S(-)-1-[2-(hydroxymethyl)oxathiolan-5-yl]cytosine, (-)-b-L-2',3'-dideoxycytidine, (-)-b-L-2',3'-dideoxy-5-fluorocytidine, (1-(2-fluoro-5-methyl-β,L-arabinofuranosyl)uracil) (FMAU), (E)-5-(2-bromovinyl)-1-β,D-arabinofuranosyluracil (BVaraU), ~~FMAU, BvaraU,~~ E-5-(2-bromovinyl)-2'-deoxyuridine, Cobucavir, trifluorothymidine (TFT), ~~TFT,~~ 5-propynyl-l-arabinosyluracil, 2'-deoxyguanosine (CDG), 2,6-diaminopurine dioxolane (DAPD), dioxolanyl-5-fluorocytosine (FDOC), 2',3'-dideoxy-2',3'-didehydrocytidine (d4C), dioxolane-guanosine (DXG), 2'-deoxy-2'-fluoroarabinofuranosyl-5-ethyluracil (FEAU), 3'-fluoro-guanosine (FLG), fluorothymidine (FLT), emtricitabine (FTC), ~~CDG, DAPD, FDOC, d4C, DXG, FEAU, FLG, FLT, FTC,~~ 5-yl-carbocyclic 2'-deoxyguanosine, Cytallene, Oxetanocin A, Oxetanocin G, Cyclobut A, Cyclobut G, fluorodeoxyuridine, 2',2'-difluorodeoxycytidine (dFdC), arabinofuranosyl cytosine (araC), ~~dFdC, araC,~~ bromodeoxyuridine, α,α,α-trifluorouridine (IDU), 2-chloro-deoxyadenosine (CdA), 2-fluoro-9-(beta-D-arabinofuranosyl)adenine (F-araA), 5-fluoro-2'-deoxyuridine-5'-monophosphate (FdUMP), ~~IDU, CdA, F-araA, 5-FdUMP,~~ Coformycin, and 2'-deoxycoformycin.

5. (Currently Amended) The compounds of ~~claim 174~~ claim 1 wherein ~~MH is~~ M is the residue of a compound selected from the group consisting of 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]-6H-purin-6-one (ACV), 9-[[2-hydroxy-1-(hydroxymethyl)-ethoxy]methyl]guanine (GCV), ~~ACV, GCV,~~ penciclovir, (R)-9-(3,4 dihydroxybutyl)guanine, and cytallene.

6. (Currently Amended) The compounds of ~~claim 174~~ claim 1 wherein $MPO_3^{2-}$ is selected from the group consisting of 9-(2-phosphonylmethoxyethyl)adenine (PMEA), 9-(2-Phosphonylmethoxyethyl)-2,6-diaminopurine (PMEDAP), (S)-1-(3-hydroxy-2-phosphonylmethoxypropyl)cytosine (HPMPC), (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine (HPMPA), (R,S)-9-(3-fluoro-2-phosphonylmethoxypropyl)adenine (FPMPA) and 9-R-2-Phosphonomethoxypropyl adenine (PMPA). ~~PMEA, PMEDAP, HPMPC, HPMPA, FPMPA, and PMPA.~~

7. (Currently Amended) The compounds of ~~claim 3~~ claim 1 wherein M is attached to the phosphorus in ~~formula~~ Formula I via an oxygen atom that is ~~in a hydroxyl group on an~~ attached to an acyclic sugar group of M.

8. (Original) The compounds of claim 7 wherein ~~MH is~~ M is the residue of a compound selected from the group consisting of 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]-6H-purin-6-one (ACV), 9-[[2-hydroxy-1-(hydroxymethyl)-ethoxy]methyl]guanine (GCV), ~~ACV, GCV,~~ 9-(4-hydroxy-3-hydroxymethylbut-1-yl)guanine, and (R)-9-(3,4-dihydroxybutyl)guanine.

9. (Original) The compounds of claim 1 wherein M is attached to the phosphorus in formula I via a carbon atom.

10. (Currently Amended) The compounds of claim 9 wherein $M\text{-}PO_3^{2-}$ is selected from the group consisting of ~~phospohonoformic~~ phosphonoformic acid, and phosphonoacetic acid.

11.-16. (Cancelled).

17. (Original) The compounds of claim 1 wherein Y is -O- located adjacent to the W' and W groups.

18. (Original) The compounds of claim 1 wherein Y is -O- located adjacent to the V group.

19. (Cancelled)

20. (Original) The compounds of claim 1 wherein

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus.

21. (Currently Amended) The compounds of claim 20 wherein V is selected from the group consisting of aryl, substituted aryl, heteroaryl, substituted heteroaryl; or

together V and W are connected via an additional 3 carbon atoms to form a cyclic substituted group containing 6 carbon atoms and mono-substituted with a substituent selected from the group consisting of hydroxyl, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy attached to one of said additional carbon atoms that is three atoms from **[[an Y]]** a Y attached to the phosphorus.

22. (Original) The compounds of claim 21 wherein V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

23. (Original) The compounds of claim 22 wherein Z, W, and W' are H; and $R^6$ is selected from the group consisting of -H, and lower alkyl.

24. (Original) The compounds of claim 23 wherein V is selected from the group consisting of aryl and substituted aryl.

25. (Original) The compounds of claim 24 wherein V is selected from the group consisting of phenyl, and substituted phenyl.

26. (Currently amended) The compounds of claim 25 wherein V is selected from the group consisting of ~~3,5-dichorophenyl~~ 3,5-dichlorophenyl, 3-bromo-4-fluorophenyl, ~~3-chorophenyl~~ 3-chlorophenyl, 3-bromophenyl, and 3,5-difluorophenyl.

27. (Original) The compounds of claim 22 wherein V is selected from the group consisting of heteroaryl and substituted heteroaryl.

28. (Original) The compounds of claim 27 wherein V is 4-pyridyl.

29. (Currently Amended) The compounds of claim 21 wherein together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and mono-substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy attached to one of said additional carbon atoms that is three atoms from [[an Y]] a Y attached to the phosphorus.

30. (Original) The compounds of claim 29 wherein together V and W form a cyclic group selected from the group consisting of $-CH_2-CH(OH)-CH_2-$, $-CH_2CH(OCOR^3)-CH_2-$, and $-CH_2CH(OCO_2R^3)-CH_2-$.

31. (Previously Amended) The compounds of claim 1 wherein V is -H, and Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, and $-CHR^2OCO_2R^3$.

32. (Original) The compounds of claim 22 wherein Z is selected from the group consisting of $-OR^2$, $-SR^2$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$ .

33. (Original) The compounds of claim 32 wherein Z is selected from the group consisting of $-OR^2$, $-R^2$ , $-OCOR^3$, $-OCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-(CH_2)_p-OR^{12}$, and $(CH_2)_p-SR^{12}$.

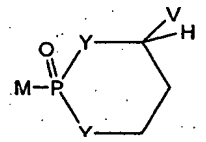
34. (Original) The compounds of claim 33 wherein Z is selected from the group consisting of $-OR^2$, -H , $-OCOR^3$, $-OCO_2R^3$, and $-NHCOR^2$.

35. (Original) The compounds of claim 22 wherein W and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

36. (Original) The compounds of claim 35 wherein W and W' are the same group.

37. (Original) The compounds of claim 36 wherein W and W' are H.

38. (Previously Amended) The compounds of claim 20 wherein said compound is of formula VI:




VI

wherein

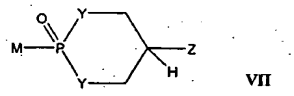
V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

39. (Original) The compounds of claim 38 wherein M is attached to phosphorus via an oxygen or carbon atom.

40. (Original) The compounds of claim 38 wherein V is selected from the group consisting of phenyl and substituted phenyl.

41. (Original) The compounds of claim 38 wherein V is selected from the group consisting of 3,5-dichlorophenyl, 3-bromo-4-fluorophenyl, 3-chorophenyl, 3-bromophenyl, and 4-pyridyl.

42. (Previously Amended) The compounds of claim 20 wherein said compound is of formula VII:




VII

wherein

Z is selected from the group consisting of:

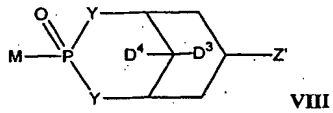
$-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OCO_2R^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OC(S)OR^3$, and $-CH_2$aryl.

43. (Original) The compounds of claim 42 wherein M is attached to the phosphorus via a carbon or oxygen atom.

44. (Original) The compounds of claim 43 wherein Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, and $-CHR^2OCO_2R^3$.

45. (Original) The compounds of claim 44 wherein $R^2$ is -H.

46. (Previously Amended) The compounds of claim 20 wherein said compound is of formula VIII:



VIII

wherein

Z' is selected from the group consisting of -OH, $-OC(O)R^3$, $-OCO_2R^3$, and $-OC(O)SR^3$;

$D^3$ is -H;

$D^4$ is selected from the group consisting of -H, alkyl, -OH, and $-OC(O)R^3$.

47. (Cancelled)

48. (Previously Amended) The compounds of claim 32 wherein W and W' are H, V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl, and Z is selected from the group consisting of -H, $OR^2$, and $-NHCOR^2$.

49. (Original) The compounds of claim 48 wherein Z is -H, and M is attached to the phosphorus of formula I via an oxygen or carbon atom.

50. (Previously Amended) The compounds of claim 49 wherein V is selected from the group consisting of phenyl and substituted phenyl.

51. (Original) The compounds of claim 49 wherein V is an optionally substituted monocyclic heteroaryl containing at least one nitrogen atom.

52. (Original) The compounds of claim 49 wherein M is attached via an oxygen atom.

53. (Original) The compounds of claim 51 wherein V is 4-pyridyl.

54. (Currently Amended) The compounds of claim 52 wherein ~~MH is~~ M is the residue of a compound selected from the group consisting of L-deoxycytidine (LdC), L-thymidine (LdT), 9-beta-D-arabinofuranosyladenine (araA), azidothymidine (AZT), stavudine (d4T), didanosine (ddI), 2',3'-dideoxyadenosine (ddA), 2',3'-dideoxycytidine (ddC), L-2',3'-dideoxycytidine (L-ddC), L-2',3'-dideoxyfluorocytidine (L-FddC), L-2',3'-dideoxy-2',3'-didehydrocytidine (L-d4C), L-2',3'-dideoxy-2',3'-didehydro-5-fluorocytidine (LFd4C), lamuvidine (3TC), ~~LdC, LdT, araA, AZT, d4T, ddI, ddA, ddC, L-ddC, L-FddC, L-d4C, L-Fd4C, 3TC,~~ ribavirin, penciclovir, 5-fluoro-2'-deoxyuridine, fialuridine (FIAU), fiacitabine (FIAC), (±)-(1α,2β,3α)-9-[2,3-bis(hydroxymethyl)cyclobutyl]-guanine (BHCG), ~~FIAU, FIAC, BHCG,~~ 2'R,5'S(-)-1-[2-(hydroxymethyl)oxathiolan-5-yl]cytosine, (-)-b-L-2',3'-dideoxycytidine, (-)-b-L-2',3'-dideoxy-5-fluorocytidine, (1-(2-fluoro-5-methyl-β,L-arabinofuranosyl)uracil) (FMAU), (E)-5-(2-bromovinyl)-1-β,D-arabinofuranosyluracil (BVaraU), ~~FMAU, BvaraU,~~ E-5-(2-

bromovinyl)-2'-deoxyuridine, Cobucavir, trifluorothymidine (TFT), ~~TFT,~~ 5-propynyl-l-arabinosyluracil, 2'-deoxyguanosine (CDG), 2,6-diaminopurine dioxolane (DAPD), dioxolanyl-5-fluorocytosine (FDOC), 2',3'-dideoxy-2',3'-didehydrocytidine (d4C), dioxolane-guanosine (DXG), 2'-deoxy-2'-fluoroarabinofuranosyl-5-ethyluracil (FEAU), 3'-fluoro-guanosine (FLG), fluorothymidine (FLT), emtricitabine (FTC), ~~CDG, DAPD, FDOC, d4C, DXG, FEAU, FLG, FLT, FTC,~~ 5-yl-carbocyclic 2'-deoxyguanosine, Cytallene, Oxetanocin A, Oxetanocin G, Cyclobut A, Cyclobut G, fluorodeoxyuridine, 2',2'-difluorodeoxycytidine (dFdC), arabinofuranosyl cytosine (araC), ~~dFdC, araC,~~ bromodeoxyuridine, α,α,α-trifluorouridine (IDU), 2-chloro-deoxyadenosine (CdA), 2-fluoro-9-(beta-D-arabinofuranosyl)adenine (F-araA), 5-fluoro-2'-deoxyuridine-5'-monophosphate (FdUMP), ~~IDU, CdA, F-araA, 5-FdUMP,~~ Coformycin, and 2'-deoxycoformycin.

55. (Currently Amended) The compounds of claim 52 wherein ~~MH is~~ M is the residue of a compound selected from the group consisting of 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]-6H-purin-6-one (ACV), 9-[[2-hydroxy-1-(hydroxymethyl)-ethoxy]methyl]guanine (GCV), ~~ACV, GCV,~~ 9-(4-hydroxy-3-hydroxymethylbut-1-yl)guanine, and (R)-9-(3,4-dihydroxybutyl)guanine.

56. (Original) The compounds of claim 49 wherein M is attached to the phosphorus via a carbon atom.

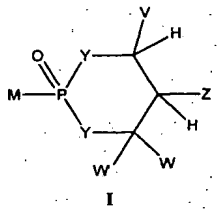
57. (Original) The compounds of claim 56 wherein V is selected from the group consisting of phenyl and 4-pyridyl and ~~MH is~~ M is the residue of a compound

selected from the group consisting of 9-(2-phosphonylmethoxyethyl)adenine (PMEA), 9-(2-Phosphonylmethoxyethyl)-2,6-diaminopurine (PMEDAP), (S)-1-(3-hydroxy-2-phosphonylmethoxypropyl)cytosine (HPMPC), (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine (HPMPA), (R,S)-9-(3-fluoro-2-phosphonylmethoxypropyl)adenine (FPMPA) and 9-R-2-Phosphono-methoxypropyl adenine (PMPA). ~~PMEA, PMEDAP, HPMPC, HPMPA, FPMPA, and PMPA.~~

58-149. (Cancelled)

150. (Currently Amended) A method of making a compound of Formula I comprising, reacting $M\text{-}P(O)L''_2$ with HY-CH(V)CH(Z)-CW(W')-YH to give the compound of Formula I,

~~a) transforming a drug having a $PO3^{2-}$ or $P(O)(NHR^6)O^-$ moiety into a compound of formula I~~:




I

wherein:

L" is a halogen;

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy,

alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V; or

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus; or

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl; or

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl; or

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH{=}CR^2_2)OH$, $-CH(C{\equiv}CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2$NHaryl, $-(CH_2)_p$-$OR^{12}$, and $-(CH_2)_p$-$SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

$R^2$ is selected from the group consisting of $R^3$ and -H;

$R^3$ is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

$R^6$ is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

$R^{12}$ is selected from the group consisting of -H, and lower acyl;

one Y is -O- and the other Y is $-NR^6-$;

M is selected from the group that attached to $PO_3^{2-}$, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent ~~but is not an FBPase inhibitor,~~ and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

~~with the provisos that:~~

~~1) M is not -NH(lower alkyl), -N(lower alkyl)$_2$, -NH(lower alkylhalide), -N(lower alkylhalide)$_2$, or -N(lower alkyl) (lower alkylhalide); and~~

~~2) $R^6$ is not lower alkylhalide;~~

~~and pharmaceutically acceptable prodrugs and salts thereof.~~

151. (Currently Amended) The method of claim 150 further comprising,

~~a)~~ converting M-$PO_3^{2-}$ to a compound M-P(O)L"$_2$ ~~wherein L" is a halogen;~~ ~~and~~

~~b) reacting M-P(O)L"$_2$ with HY-CH(V)CH(Z)-CW(W')-YH~~.

152. (Original) The method of claim 151 wherein HY-CH(V)CH(Z)-CW(W')-YH is chiral.

153. (Currently Amended) The method of claim 152 further comprising isolating a single diastereomer of the compound having Formula I.

154. (Cancelled)

155. (Previously Amended) The method of claim 166 wherein L-P(-YCH(V)CH(Z)-CW(W')Y-) is chiral.

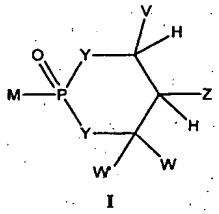
156. (Currently Amended) The method of claim 155 wherein the chiral ~~phosphoramidite~~ compound is generated using a chiral amino alcohol.

157. (Original) The method of claim 155 wherein said oxidizing agent produces a single stereoisomer at the phosphorus.

158–164. (Cancelled)

165. (Previously Amended) The compounds of claim 1 wherein V and M are *cis* to one another on the phosphorus-containing ring of Formula I.

166. (Currently Amended) ~~The~~ A method of making a compound of ~~formula I~~ Formula I:



I

comprising

a) converting a hydroxyl or amino on M to a phosphoramidite by reaction with L-P(-YCH(V)CH(Z)-CW(W')Y-) wherein L is selected from the group consisting of $NR^1_2$ and halogen; and

b) transforming said phosphoramidite into a compound of formula I by reaction with an oxidizing agent;

wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V; or

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy,

alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus; or

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing [[one]] 1 heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl; or

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl; or

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, -OCOR3, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2$NHaryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

each $R^1$ is independently selected from the group consisting of alkyl, aryl, and aralkyl or together $R^1$ and $R^1$ form a cyclic group, optionally containing a heteroatom;

$R^2$ is selected from the group consisting of $R^3$ and -H;

$R^3$ is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

$R^6$ is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

$R^{12}$ is selected from the group consisting of -H, and lower acyl;

one Y is -O- and the other Y is $-NR^6-$; and

M is selected from the group that attached to $PO_3^{2}$, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent ~~but is not an FBPase inhibitor,~~ and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

~~with the provisos that:~~

~~1) M is not -NH(lower alkyl), -N(lower alkyl)$_2$, -NH(lower alkylhalide), -N(lower alkylhalide)$_2$, or -N(lower alkyl) (lower alkylhalide);~~

~~2) $R^6$ is not lower alkylhalide; and~~

~~3) $R^1$ is not methyl.~~

167.-170. (Cancelled)

171. (Currently Amended) The compounds of claim 1, wherein:

W and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl;

V is selected from the group of aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2$NHaryl, $(CH_2)_p$-$OR^{12}$, and $-(CH_2)_p$-$SR^{12}$; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

p is an integer 2 or 3;

$R^2$ is selected from the group consisting of $R^3$ and -H;

$R^3$ is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

$R^6$ is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

$R^{12}$ is selected from the group consisting of -H and lower acyl; and

one Y is -O- and the other Y is -$NR^6$-;

~~M is selected from the group that attached to $PO_3^{2-}$, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;~~

~~with the provisos that:~~

~~1) M is not NH(lower alkyl), N(lower alkyl)$_2$, NH(lower alkylhalide), N(lower alkylhalide)$_2$, or N(lower alkyl) (lower alkylhalide); and~~

~~2) $R^6$ is not lower alkylhalide;~~

and pharmaceutically acceptable prodrugs and salts thereof.

172. (Currently Amended) The compounds of claim 1, wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1 -alkynyl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-SR^2$, and $-CH_2$NHaryl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus;

$R^2$ is selected from the group consisting of $R^3$and -H;

$R^3$ is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

$R^6$ is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl; and

one Y is -O- and the other Y is $-NR^6-$;

~~M is selected from the group that attached to $PO_3^{2-}$, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;~~

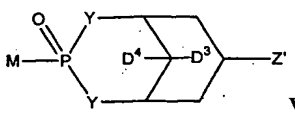
~~with the provisos that:~~

~~1) M is not NH(lower alkyl), N(lower alkyl)$_2$, NH(lower alkylhalide), N(lower alkylhalide)$_2$, or N(lower alkyl) (lower alkylhalide); and~~

~~2) $R^6$ is not lower alkylhalide;~~

and pharmaceutically acceptable prodrugs and salts thereof.

173. (Currently Amended) The compounds of claim 1 that are of formula VIII




VIII

wherein:

Z' is selected from the group consisting of -OH, $-OCO_2R^3$, $-OC(O)R^3$, and $-OC(O)SR^3$;

$R^2$ is selected from the group consisting of $R^3$ and -H;

$R^3$ is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

$R^6$ is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

one Y is -O- and the other Y is $-NR^6-$;

$D^3$ is -H;

$D^4$ is selected from the group consisting of -H, alkyl, -OH, $-OR^2$ and [[$-OC(O)R^3$.]] $-OC(O)R^3$; and

~~M is selected from the group that attached to $PO_3^{2-}$, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;~~

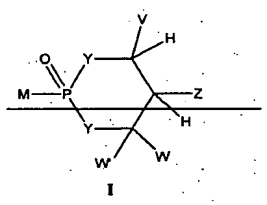
~~with the provisos that:~~

~~1) M is not -NH(lower alkyl), $-N(\text{lower alkyl})_2$, -NH(lower alkylhalide), $-N(\text{lower alkylhalide})_2$, or -N(lower alkyl) (lower alkylhalide); and~~

~~2) $R^6$ is not lower alkylhalide;~~

and pharmaceutically acceptable prodrugs and salts thereof.

174. (Currently Amended) The compound of ~~formula I:~~ claim 1, wherein




I

~~wherein:~~

~~V, W, and W' are independently selected from the group consisting of H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or~~

~~together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or~~

~~together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;~~

~~together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;~~

~~together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing [[one]]~~ 1 ~~heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;~~

~~together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;~~

~~Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$,~~

~~$-CHR^2N_3$, $-CH_2$aryl, $-CH$(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2$NHaryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;~~

~~p is an integer 2 or 3;~~

~~with the provisos that:~~

~~a) V, Z, W, W' are not all H; and~~

~~b) when Z is $R^2$, then at least one of V, W, and W' is not H, alkyl, aralkyl, or alicyclic;~~

~~$R^2$ is selected from the group consisting of $R^3$ and H;~~

~~$R^3$ is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;~~

~~$R^6$ is selected from the group consisting of H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;~~

~~$R^{12}$ is selected from the group consisting of H, and lower acyl;~~

~~one Y is O and the other Y is $NR^6$;~~

M is a nucleoside ~~that attached to $PO_3^{2-}$, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;~~

~~with the proviso that $R^6$ is not lower alkylhalide;~~

~~and pharmaceutically acceptable prodrugs and salts thereof~~.

175. (New) The compound of claim 174, wherein M is the residue of an antiviral nucleoside, L-nucleoside, acyclic nucleoside, dideoxy nucleoside, arabinofuranosyl nucleoside, carbocyclic nucleoside, nucleoside having a fluorinated sugar or dioxolane nucleoside.